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ACUTE LUPUS ERYTHEMATOSUS WITH COMPLETE DEFICIENCY OF THE C_4 FRACTION OF COMPLEMENT

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16. Abstract

A new symptom of acute disseminated lupus erythematosus and a complete heredity deficiency in one of the fractions of the complement were isolated. The subject was treated with cortisone and hydroxychloroquine and all the cutaneous lesions disappeared but the complement assays continue to show complete absence of C_4.

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ACUTE LUPUS ERYTHEMATOSUS WITH COMPLETE DEFICIENCY OF THE C_4 FRACTION OF COMPLEMENT

G. Hauptman, E. Grosshans, E. Heid, S. Mayer and A. Basset

Following the recent publication in the literature of obser- /881* vations of several cases of lupus syndrome with a heredity deficiency of certain complement fractions: C1r(1), C1s(2), C2 (3,4) and inhibitor of C(1) esterase (5), it is possible to isolate a new syndrome consisting of an association between acute disseminated lupus erythematosus (ADLE) and a complete deficiency in one of the fractions of the complement.

We have been able to study a case of ADLE in which there was a complete deficiency in the C_4 fraction of complement, an as yet unpublished association (6).

An 18 year old girl, with no particular history, was admitted on 2/2/73 for ADLE. Cutaneous lesions began on the face in August 1972 after a period of prolonged exposure to the sun, and their appearance was perhaps partially caused by oral intake of contraceptives for two years. ADLE symptoms present were accelerated "VS" (sedimation rate), elevated fibrinemia, cryoglobulinemia (IgM-IgG-C1q), serial anticomplement activity, signs of renal involvement (protein urea, microscopic hematuria), positive rheumatoid serology, presence of serial lymphocytotoxins. But, as in most published cases, the biological signs most characteristic of ADLE were lacking, LE cells, antinuclear antibodies, hypergammaglobulinemia. The cutaneous biopsy is characteristic of ADLE but examination of the sections by immunofluorescence showed no immunoglobulin deposits or C3 at the level of dermoepidermic function.

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*Numbers in the margin indicate pagination in the foreign text.

The analysis of complement revealed complete absence of hemolytic activity in the serum as well as a practically zero titer of complement by immunoadherence measurement. The absence of globular complement activity could be related to a complete absence of the C4 fraction (beta-1E globulin), an abnormality observed consistently over a period of ten months. The C1, C2, C3 and C5 fractions were found regularly and measured. The absence of C4 was verified by immunohemolysis techniques and confirmed indirectly by the ability of the patient's serum to lyse red cells carrying C4 (EAC4). Moreover, addition of purified human C4 (Lab. Cordis, Miami, USA) to the serum allowed complete restoration of the hemolytic activity of the serum.

The so-called "alternate" activation pathway of complement (7) has been explored by measurement of the proactivator of C_3 (C3PA) and by a study of the transformation of C3 and C3PA after incubation of the serum with inulin. The C3PA-titer is normal, and transformation of C3 is normal after incubation with inulin. However, degradation does not take place if one incubates the serum with clumped IgG. These results confirm the existence of a block in the classical activation pathway of C3 due to the absence of C_4 while the alternative pathway is functional.

The polynucleated cells of the patient are incapable of phagocytizing latex particles while the patient's serum, but this problem is corrected by the addition of fresh normal human serum.

The inhibitor of C1 esterase is present (assay by immunodiffusion): the patient never showed clinical manifestations of hereditary angioneurotic edema, a disease in

which the C4 titer drops dramatically during edema attacks.

A complete familial history was not worked out but we did find in the mother on two occasions a C4 titer reduced to half the average normal value. Under these conditions the hypothesis of a partial deficiency (heterozygous) in the mother and a total one in the ill daughter (homozygous) may be advanced. Such a complete deficiency in the C4 fraction has not yet been described in man; only a functional deficiency in the C4 molecule was discovered in Japan (8).

The patient was treated with cortisone and hydroxychloroquine and all the cutaneous lesions disappeared but the complement assays continue to show complete absence of C4.

This case underscores once more the role of complement in ADLE and raises the problem of the hereditary aspect of lupus. It is striking to note that the cases described all /882
involve a deficiency in the constituents of complement in the classical activation pathway of C3 (C1, C4, and C2), and the hypothesis of hyperfunctioning of the alternate pathway has been advanced (1) in order to explain the pathologic manifestations found in these patients. It is known that the alternate pathway occurs in classical ADLE (9). One may nonetheless point out, in encountering this hypothesis, the absence of obvious signs of hypercatabolism of C3 in our patient (no decrease in titer of either C3 or C3PA).

One might think that such a deficiency in complement, hobbles cellular defense mechanisms against infections, lowers normal antibody production, and can predispose to latent chronic viral infection (3) or predispose to

drug or light sensitization. In a recently described case of C2 deficiency with anaphylactic purpura (10) some morphologic structures identified as mycoplasma have been found in the serum.

These cases should inspire efforts to carry out a more complete study of complement in the atypical forms of ADLE as well as in the familiar forms.

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